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ABSTRACT

The soft lithography fabrication technique was applied to three microfluidic devices. The method was used to create an original micropump design and retrofit to existing designs for a DNA manipulation device and a counter biological warfare sample preparation device. Each device presented unique and original challenges to the soft lithography application. All design constraints of the retrofit devices were satisfied using PDMS devices created through variation of soft lithography methods. The micropump utilized the versatility of PDMS, creating design options not available with other materials. In all cases, the rapid processing of soft lithography reduced the fabrication time, creating faster turnaround for design modifications.

INTRODUCTION

Three microfluidic systems were fabricated using the soft lithography process developed by Whitesides et al. [1]. The flexibility afforded by this technique enabled the fulfillment of various design constraints encountered with the different devices. In all cases, glass substrates were photolithographically patterned using wet chemical etching to form masters for molding PDMS (Sylgard 184, Dow Corning). The PDMS was bonded to either glass or PDMS substrates to create sealed channels, using an ethanol clean and oxygen plasma surface treatment. For two devices, electrodes were patterned on the glass substrates. Metallization was also successfully demonstrated on PDMS using an e-beam evaporated chromium adhesion layer and gold conductive film, with patterning accomplished using a shadow mask. Fluidic connections were made by boring holes through the PDMS, or by imbedding connectors in the PDMS during molding. The objective for application of soft lithography was to develop an approach for fast turn-around of new flow cell designs. In the first application, merging laminar flow microchannels were fabricated for single molecule DNA manipulation and processing. In the second application devices were made in conjunction with a counter biological warfare project aimed at developing a miniaturized sample preparation module. Difficulties in glass-glass bonding and polymer based fusion bonding inspired the use of PDMS as the substrate for the modules. In the final example a piezo-electric actuated micropump prototype was fabricated within four days of conceptualization. Each application required other various deviations from the standard soft lithography process to satisfy the functional requirements of each device.

DEVELOPMENT

DNA manipulation

Single molecule DNA manipulation and processing were accomplished using merging laminar flow channels fabricated in PDMS via soft lithography. Brewer et al. [2] developed this technique using glass flow cells to demonstrate protamine induced condensation and decondensation of single DNA molecules. A dual port flow cell was used to introduce two solutions into the device. The microscale fluid dynamics produced laminar flow in both solutions, thereby avoiding mixing in the merged channel. An optical trap was used to capture individual glass flow cells and transfer them into the protamine flow. Protamine induced condensation of the DNA molecule, and decondesation was accomplished by moving the DNA molecule back into the non-protamine flow.

The original devices used for the project consisted of a thin slide cover bonded over 1mm wide by 40 μm deep channels etched into a microscope slide. Fluid connection were made via tubing connectors epoxied at the inlet and outlet ports. The testing apparatus was designed to facilitate the use of these glass devices and thus established the design requirements for the PDMS devices. The use of the laser trap required low background fluorescence from the substrate material to ensure adequate focusing for molecule capturing. The thin coverslip used to cover the flow channels was necessary due to the confocal microscope used for experimental observations. Leak-proof connections were also desirable to ensure accurate flow control. The use of soft lithography for this application was dependent on the fulfillment of these requirements.

Low background fluorescence was achieved by using a "space grade" PDMS material. This material lacks the typical PDMS contaminants, reducing the amount of disturbances to the optic laser light. Thin coverslips necessary for the confocal lens were also integrated into the PDMS device. Coverslips were first rinsed with ethanol, then surface treated with an oxygen plasma before being bonded over the molded PDMS channels. Leak-proof fluidic connections were formed by imbedding the connectors in PDMS as it was being poured onto the mold. Once the polymer had cooled, the connectors were sealed tightly into the device.

The PDMS devices not only satisfied the desired design requirements, but produced other advantages as well. Soft lithography reduced the fabrication process time from weeks to less than three days. This processing improvement provided the ability to progress rapidly from new design concepts to device prototypes. The accelerated process was due to multiple device fabrication from single molds, and decreased complexity of creating molded channels in PDMS versus etching them in glass. Depth variations were created using multiple shadow masks during photolithography of the mold. With these alterations in the depth of channels velocity was varied and clogging reduced.

Counter Bio-Warfare

Preparation of environmental samples for biological testing was accomplished using a microfluidic module fabricated employing soft lithography. The project's goal was to miniaturize an ATM sized, automated system that collects airborne particles, prepares the samples, and performs a flow cytometry assay. A miniaturized system requires functionality including focusing, trapping, filtering, pre-concentrating, mixing, pumping, and valving.

Wang et al. [3] developed a microfluidic device to perform sample preparation for the aforementioned miniaturized system. Their platform was developed to perform mixing and collection for a bead-based flow cytometry immunoassay format and DNA concentration and purification for PCR analysis. Interdigitated electrodes were patterned at the bottom of microchannels to utilize dielectrophoretic (DEP) particle capture for concentrating and purifying the samples. Channels molded into PDMS were bonded over the integrated electrodes. Magnetohydrodynamic (MHD) pumping was used to pump and switch fluid through the flow channels in the system.

Two substrates were used in fabrication of the original Wang et al. sample preparation modules. Experimentation was done with both glass-glass and acrylic devices. Channels were etched into the substrate using standard photolithography techniques. The electrodes necessary for DEP were patterned into the channels using a shadow mask to specifically apply an e-beam evaporated chromium adhesion layer and gold conductive film. Both substrates required high temperature bonding, and acrylic devices required high pressures as well. Fluidic connections were made through o-ring sealed connectors threaded into a specially designed device package.

Consequent application of soft lithography to the sample preparation modules was induced by challenges encountered with the previous materials. Collapsing channels, inherent in glass-glass and polymer based fusion bonding, caused shorts in the patterned electrodes. It was also observed that proteins in the injected samples were adherent to the glass walls. The fabrication of the original devices was a relatively long process, eliminating the ability to quickly test new design modification.

The PDMS device consisted of channels etched into a glass substrate with electrodes patterned into these channels. Covalent bonding of glass to PDMS was achieved through an ethanol wash and oxygen plasma treatment of the surfaces. This room temperature bond avoided collapse of the microchannels. Protein adherence along the channels walls was negligible for the PDMS material, eliminating the previous complications. Soft lithography reduced the fabrication process time dramatically as well. The accelerated process was due to multiple device fabrication from single molds, and the replacement of complicated bonding procedures.

Though the PDMS-glass device was selected as most appropriate for this application, the capabilities of the material allowed for testing of other combinations. PDMS-acrylic and PDMS-PDMS devices were also experimented with. Using a silicon rich vapor proceeded by oxygen plasma surface treatment, PDMS was successfully bonded to acrylic. Etching of the microchannels however, was less time intensive in glass than in acrylic. The use of a PDMS-PDMS device was dependent on the ability to apply patterned electrodes to the surface. Metallization of the PDMS surface was successfully demonstrated using an e-beam evaporated chromium adhesion layer and gold conductive film, with patterning accomplished using a shadow mask. The glass-PDMS device provided a much stiffer module and was therefore preferred over the PDMS-PDMS design.

Micropump

Micropumps are essential in microfluidics to provide complete miniaturization and integration of microfluidic systems. Because of high demand for these micropumps, a multitude

of pump designs exist. Comparable features of micropump designs include size, maximum flow rate, and pressure losses associated with valve leakage. A micropump that adequately satisfies these criteria would be applicable to a wide range of microfluidic systems including the DNA manipulation device and bio-warfare device. The desire for such a pump and success of soft lithography in other applications was the inspiration for the PDMS micropump.

The micropump was fabricated using soft lithography techniques for glass-PDMS devices. Two collinear channels were photolithographically etched at a depth of 40 μm into the glass. A non-etched region remained to separate the channels. An e-beam evaporated chromium adhesion layer and gold conductive film were patterned between the channels using a shadow mask. Flow channels were enclosed and the pump membrane created with a 250 μm PDMS sheet bonded over the glass. A bi-morph piezo was placed over the membrane in the patterned region. Pre-cured PDMS was then poured over the entire device to create the backing for the piezo and channels.

Design of this micropump utilizes the versatility of the PDMS-glass, creating design options not available with other materials. Creation of the 250 mm sheet was accomplished by pressing liquid PDMS between two glass pieces and curing. This process provides a means of accurately varying the thickness of the pump's membrane. Because of selective bonding, the membrane does not bond to the gold conductive film between the channels. The pump also takes advantage of the fact that pre-cured PDMS added as a backing to the piezo will adhere to the PDMS membrane. The more complicated soft lithography methods applied to the fabrication of the micropump, still provided an observable prototype within 5 days.

The function of the micropump if based on peristaltic motion of multiple membranes. The original prototype was designed with only one membrane to test the design principle. As seen in Figure 1, the piezo-electric disk provides a moment on he membrane when a voltage is applied. Due to selective bonding, the membrane releases from the gold region, creating a flow path. When the voltage is removed, or becomes negative as in AC current, the membrane returns to its normally closed position. Using three or more actuators, peristaltic motion can be created to push fluid through the channels.

Tests of the one actuator design found failures due to channel blockages caused by bonding inside the channels. Creation of the central flow path was recorded however with application of a low frequency AC current. Simple process modifications will eliminate future blockages and allow for testing of attainable flow rates and pressures in the pump.

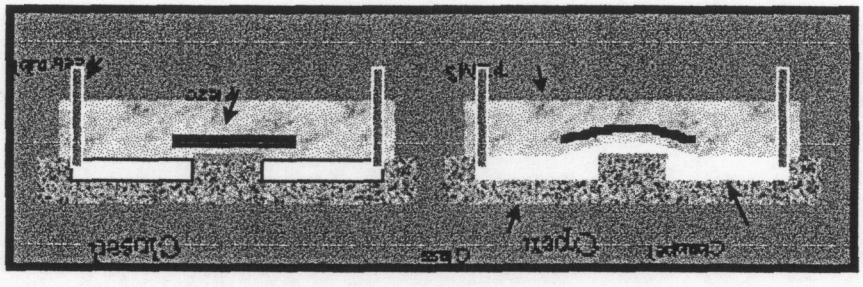

Figure 1

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REFERENCES

1. D. C. Duffy, J. C. McDonald, O. Schueller, G. M. Whitesides, Analytical Chemistry 70 (1998) 4974
2. R.L. Brewer, M. Corzett, and R. Balhorn, Science 286 (1999) 120
3. A. W. Wang, W. J. Benett, L. A. Tarte, K. S. Venkateswaran, ASME International Mechanical Engineering Congress and Exposition, Orlando, Florida, Nov. 2000.